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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,538	09/15/2005	Ian Richard Matthews	003301-231	4769

21839 7590 07/14/2009

BUCHANAN, INGERSOLL & ROONEY PC
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EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
07/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/537,538	MATTHEWS ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-21* is/are pending in the application.

4a) Of the above claim(s) *9,10,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11-16,19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants have not amended the claims to the elected group. Y being a N group.

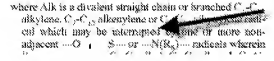
Applicants have elected Group I of the restriction, claims 1-7,11-16, 19-21 drawn to formula I wherein Y is N.

Response to arguments

The rejection of claims 1-7, 11-16, 19-21, under 35 USC 102 over Matthews et al 7291612 and 7081456 has been withdrawn but modified to a 103 rejection. The reference clearly teaches the compounds generically. Applicants argue that Z is always a carboxylic acid or an ester and the prior art has it always connected to an N .

This is incorrect. The prior art '612 on columns 55 and 56, has various definitions. R4 can be NR7C=OR6 . R6 can be alkyl-Q. See claim 8 wherein Q is -COOCH3.

First of all the alkyl itself may be interrupted by heteroatoms, see column 56.



and Q can be an ester.

This would read on the compounds when X is a NHCOCH2-O-CH2 and Z is an ester.

Thus the arguments presented by the applicants is not convincing.

The rejection of the claims 1-7,11-16, 19-21 under ODP over 7291612, 7081456 still stands as applicants have not provided a TD over these patents..

The rejection of the claims 1-7,11-16,19 and 20 under 35 USC 103 over Bjork et al WO 03/004495, US 6642249 still stands. Even though applicants may have amended the claims to have R2 to be substituted cycloalkyl and optionally substituted C7 cycloalkyl

and phenyl, the substituent is an alkyl, and H v alkyl is a prima facie obvious modification.

So the examiner has maintained all the rejections and made this action FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 11-16, 19 - 21 are rejected under 35 U.S.C. 103(a) as being obvious over by US 7291612 and US 7081456. Mattews et al .

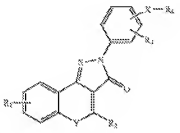
The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance

with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

See claims of the US 7291612

1. A compound of formula (I) or a pharmaceutically or veterinarily acceptable salt thereof:

(I)



wherein

R_1 and R_2 independently represent H; F; Cl; Br; —NO_2; —CN; C_1-C_6 alkyl optionally substituted by F or Cl; or C_1-C_6 alkoxy optionally substituted by F;

R_3 represents H, or optionally substituted C_1-C_6 alkyl, C_3-C_7 cycloalkyl or optionally substituted phenyl;

Y represents —O—, —S—, N-oxide, or —$N(R_5)$— wherein R_5 represents H or C_1-C_6 alkyl;

X represents a bond or a divalent C_1-C_6 alkylene radical;

R_4 represents —$NR_6C(=O)R_6$, —$NR_6C(=O)OR_6$, —$NHC(=O)NHR_6$ or —$NHC(=S)NHR_6$ wherein:

when R_4 represents —$NR_6C(=O)R_6$ or —$NR_6C(=O)OR_6$, R_6 represents H, or a radical of formula —$(Alk)_b$-Q wherein b is 0 or 1 and Q represents H; —CF_3; —OH; —SH; —NR_8R_8 wherein each R_8 may be the same or different, an ester group; or an optionally substituted phenyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl or heterocyclic ring having from 5 to 8 ring atoms;

when R_4 represents —$NHC(=O)NHR_6$, or —$NHC(=S)NHR_6$, R_6 represents a radical of formula —$(Alk)_b$-Q wherein b is 1 and Q represents —CF_3; —OH; —SH; —NR_8R_8 wherein each R_8 may be the same or different; an ester group; or an optionally substituted phenyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl or heterocyclic ring having from 5 to 8 ring atoms;

where Alk is a divalent straight chain or branched C_1-C_{12} alkylene, C_2-C_{12} alkenylene or C_2-C_{12} alkynylene radical which may be interrupted by one or more non-adjacent ---O---, ---S--- or ---N(R_8)--- radicals wherein R_8 represents H or C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, or C_3-C_6 cycloalkyl, and

R_7 represents H or C_1-C_6 alkyl; or when taken together with the atom or atoms to which they are attached R_6 and R_7 form an optionally substituted heterocyclic ring having from 5 to 8 ring atoms.

2. A compound as claimed in claim 1 wherein R_1 is H, F, Cl, methyl or methoxy.

3. A compound as claimed in claim 1 wherein R_2 is H, methyl, cyclopropyl, phenyl, or fluoro-, chloro-, methyl-, or methoxy-substituted phenyl.

4. A compound as claimed in claim 1 wherein R_3 is H, F, Cl, methyl, or methoxy.

5. A compound as claimed in claim 1 wherein Y is ---O---, ---S---, or ---N(R_5)--- wherein R_5 represents H or methyl.

6. A compound as claimed in claim 1 wherein X is a bond, or a ---CH_2---, or ---CH_2CH_2--- radical.

7. A compound as claimed in claim 1 wherein R_4 represents ---$NR_6C(=O)R_{6a}$, ---$NR_6C(=O)OR_{6a}$, ---$NHC(=O)NHR_6$ or ---$NHC(=S)NHR_6$, wherein:

when R_4 represents ---$NR_6C(=O)R_6$ or ---$NR_7C(=O)OR_{6a}$, R_6 is H or a radical of formula ---Alk_b-Q wherein b is 0 or 1 and

Alk is a ---$(CH_2)_n$---, ---$CH((CH_2)_mCH_3)(CH_2)_n$---, ---$CH((CH_2)_mCH_3)((CH_2)_pCH_3)(CH_2)_n$---, ---$(CH_2)_nO(CH_2)_m$---, or ---$(CH_2)_nO(CH_2)_pO(CH_2)_m$---, radical where n is 1, 2, 3 or 4 and m and p are independently 0, 1, 2, 3 or 4, and Q represents H, ---OH, ---$COOCH_3$, phenyl, cyclopropyl, cyclopentyl, cyclohexyl, pyridyl, furyl, thienyl, or oxazolyl, and

when R_4 represents ---$NHC(=O)NHR_6$ or ---$NHC(=S)NHR_6$, R_6 is a radical of formula ---Alk_b-Q wherein b is 1 and

Alk is a ---$(CH_2)_n$---, ---$CH((CH_2)_mCH_3)(CH_2)_n$---, ---$CH((CH_2)_mCH_3)((CH_2)_pCH_3)(CH_2)_n$---, ---$(CH_2)_nO(CH_2)_m$---, or ---$(CH_2)_nO(CH_2)_pO(CH_2)_m$--- radical, where n is 1, 2, 3 or 4 and m and p are independently 0, 1, 2, 3 or 4, and Q represents ---OH, ---$COOCH_3$, phenyl, cyclopropyl, cyclopentyl, cyclohexyl, pyridyl, furyl, thienyl, or oxazolyl, and

R_7 is H, or when taken together with the nitrogen atom to which they are attached R_6 and R_7 form a pyrrolidine-2-one or pyrrolidine-2,5-dione ring.

8. A compound as claimed in claim 1 wherein R_1 is H, F, or Cl; R_2 is H; R_3 is H, F, or Cl; Y is ---NH---; X is a bond; and R_4 represents ---$NR_6C(=O)R_{6a}$, ---$NR_6C(=O)OR_6$ or ---$NHC(=O)NHR_6$ wherein:

when R_4 represents ---$NR_6C(=O)R_6$ or ---$NR_7C(=O)OR_{6a}$, R_6 is H or a radical of formula ---Alk_b-Q wherein b is 0 or 1 and

Alk is a ---$(CH_2)_n$---, ---$CH((CH_2)_mCH_3)(CH_2)_n$---, ---$CH((CH_2)_mCH_3)((CH_2)_pCH_3)(CH_2)_n$---, ---$(CH_2)_nO(CH_2)_m$---, or ---$(CH_2)_nO(CH_2)_pO(CH_2)_m$--- radical where n is 1, 2, 3 or 4 and m and p are independently 0, 1, 2, 3 or 4, and Q represents H, ---OH, ---$COOCH_3$, phenyl, cyclopropyl, cyclopentyl, cyclohexyl, pyridyl, furyl, thienyl, or oxazolyl, and

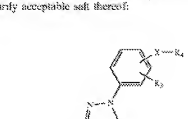
when R_4 represents ---$NHC(=O)NHR_{6a}$, R_6 is a radical of formula ---Alk_b-Q wherein b is 1 and

Alk is a ---$(CH_2)_n$---, ---$CH((CH_2)_mCH_3)(CH_2)_n$---, ---$CH((CH_2)_mCH_3)((CH_2)_pCH_3)(CH_2)_n$---, ---$(CH_2)_nO(CH_2)_m$---, or ---$(CH_2)_nO(CH_2)_pO(CH_2)_m$---,

And US 7081456.

The invention claimed is:

1. A compound of formula (I) or a pharmaceutically or veterinarily acceptable salt thereof:



wherein

R_2 and R_3 independently represent H; F; Cl; Br; —NO_2; —CN; C_1–C_6 alkyl optionally substituted by F or Cl; or C_1–C_6 alkoxy optionally substituted by F;

R_4 represents H, or optionally substituted C_1–C_6 alkyl, C_3–C_7 cycloalkyl or optionally substituted phenyl;

Y represents —O—, —S—, N-oxide, or —$N(R_5)$— wherein R_5 represents H or C_1–C_6 alkyl;

X represents a bond or a divalent C_1–C_6 alkylene radical;

R_1 represents —C(=O)NR_aR_b, wherein

R_a represents a radical of formula -(Alk)$_b$-Q wherein b is 1 and

Alk is an optionally substituted divalent straight chain or branched C_1–C_{12} alkylene, C_2–C_{12} alkenylene or C_2–C_{12} alkynylene radical which may be interrupted by one or more non-adjacent —O—, —S— or —$N(R_c)$— radicals wherein R_c represents H or C_1–C_4 alkyl, C_3–C_6 alkenyl, C_3–C_6 alkynyl, or C_3–C_6 cycloalkyl, and

Q represents H; —CF_3; —OH; —SH; —NR_dR_e wherein each R_d may be the same or different, an ester group, or an optionally substituted phenyl, C_3–C_7 cycloalkyl, C_3–C_7 cycloalkenyl or heterocyclic ring having from 5 to 8 ring atoms; and

R_b represents H or C_1–C_6 alkyl; or when taken together with the atom or atoms to which they are attached R_a and R_b form an optionally substituted heterocyclic ring having from 5 to 8 ring atoms.

2. A compound as claimed in claim 1 wherein R_1 is H, F, Cl, methyl or methoxy.

3. A compound as claimed in claim 1 wherein R_2 is H, methyl, methoxy, cyclopropyl, phenyl, or fluoro-, chloro-, methyl, or methoxy-substituted phenyl.

4. A compound as claimed in claim 1 wherein R_3 is H, F, Cl, methyl, or methoxy.

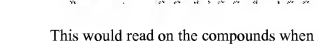
5. A compound as claimed in claim 1 wherein Y is —O—, —S—, or —NR_5— wherein R_5 represents H or methyl.

6. A compound as claimed in claim 1 wherein X is a bond, or a —CH_2— or —CH_2CH_2— radical.

7. A compound as claimed in claim 1 wherein R_a represents —C(=O)NR_{2b} wherein R_b is a radical of formula -Alk_2-Q wherein

The prior art '612 on columns 55 and 56, has various definitions. R4 can be NR7C=OR6 . R6 can be alkyl-Q. See claim 8 wherein Q is -COOCH3.

First of all the alkyl itself may be interrupted by heteroatoms, see column 56.


where Alk is a divalent straight chain or branched C_1-$C_{...}$ alkylene, C_2-C_{12} alkenylene or $C_{...}$ radical which may be interrupted by one or more non-adjacent —O— , —S— or —$NR_{...}$— radicals wherein

and Q can be an ester.

This would read on the compounds when X is a NHCOCH2-O-CH2 and Z is an ester.

The generic teaching is there and hence it would be obvious to modify the claims to obtain the claims of the invention. The prior art teaches the R2 to be optionally substituted phenyl and that is what applicants claim read. Compounds are very similar and the difference is in the X and Z position and the a finite number of options are given in the prior art so it would be obvious to modify the compounds using the given variables to obtain the compounds of the invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either

is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 11-16 , 19-21 are rejected on the ground of nonstatutory double patenting over claims 1-8 of U. S. Patent No. 7291612 , and claims 1-7 of US 7081456 .

Claims 1-7, 11-16, 19 -21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, of U.S. Patent No. US 7291612 and claims 1-7 of US Patent No. 7081456.. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is overlapping subject matter.

See rejection above.

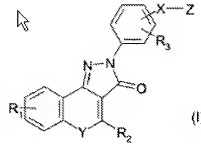
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 11-16, 19 -21 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 03/004495 (filing date) Bjork et al. US 6642249. (July 2001)

Applicants claims are drawn to compounds and pharmaceutical compositions of the formula

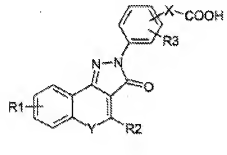


(I)

wherein Z is a COOH or an ester thereof., R2 is an optionally substituted cycloalkyl or a phenyl

Scope & Content of Prior Art MPEP 2141.01

WO 03/004495 Bjork et al teaches compounds of the formula



(I)

Y is a NR4, R2 is a H or a lower alkyl. (wherein lower alkyl meaning includes cyclic alkyl groups having 1-6 carbon atoms (see line 9 and 10 page 4 of the reference.

Difference between Prior Art and the claims MPEP 2141.02

Even though WO '495 Bjork et al teaches the same core of the same use, it generically teaches R2 being a cycloalkyl. Applicants compounds now have the cycloalkyl to be substituted . The substituents can be an alkyl also.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

Bjork et al generically teaches the same core with Z being a COOH or its ester.

Even though no species have been made the teaching that a cycloalkyl ring can be present at the R2 substitution and still retain the properties. Thus motivating a person of skill in the art to substitute a carbocyclic ring for R2 (cycloalkyl or a phenyl) and still have some expectation of success that the compounds would have activity. KSR International v Telflex Inc. In the absence of unexpected results it is prima facie obvious.

Claim Objections

Claim1 has X to be NH(CO)C1-5alkyl objected to because of the following informalities: It cannot be seen where Z would be attached as all the valency are ful. Appropriate correction is required.

Conclusion

Claims 1-7, 11-16, 19 and 20,21 are not allowable.

Claims 9, 10, 17, 18 are withdrawn as non-elected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the

advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

July 8, 2009